

Low Doses of Zinc Gluconate for Inflammatory Acne

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The effect of zinc on acne is unclear. In this study, only patients with an inflammatory acne were included in a double-blind trial using low doses of zinc gluconate (200 mg/day, corresponding to 30 mg zinc metal). We obtained a significantly different result between zinc and placebo groups in the inflammatory score ($p < 0.02$). This efficiency could be explained by the action of zinc on inflammatory cells, especially granulocytes.

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Subsequent to an initial report by Michaëlsson (1), several publications have either proved or discounted the effectiveness of zinc therapy on acne. This disparity can be attributed to two factors: firstly, by whether the type of acne treated is inflammatory or not; and secondly, by the zinc dose administered. Accordingly, we carried out a multicentre double-blind trial in 66 patients with inflammatory acne, involving use of low doses of zinc.

MATERIAL AND METHODS

Patients

Sixty-six patients (39 men and 27 women) gave their informed consent to take part in the study. All subjects had at least 15 pustules and/or nodules with inflammatory reaction. Those with liver or kidney involvement were excluded. None had received medical treatment for acne during the 4 weeks preceding the study, and no medication that might interfere with the results (penicillamine, cyclines, oestrogens, anti-androgens), was allowed during the study. Locally, patients could use only a cleansing soap.

Treatment

Patients were randomly assigned to two groups depending on whether they were given a coded medication in the form of zinc gluconate capsules [(100 mg zinc gluconate corresponding to 15 mg Zn⁺⁺) Labcatal*], or placebo capsules (lactose). Two capsules per day were given 20 min before breakfast over a 2-month period.

Examination procedure

Each patient was examined before and after 1 and 2 months of treatment, according to the following procedures:

1) *Determination of the inflammatory score.* The number and type of lesions (papules, pustules and nodules) were counted on the face, back and chest. Lesion severity in each region was scored as follows: 1) 1 to 5 lesions; 2) 6 to 10 lesions; 3) 11 to 20 lesions; 4) more than 20 lesions. Comedones were not counted.

To facilitate overall estimation of the inflammatory factor, each type of lesion was assigned an inflammatory index: ($\times 5$ for nodules, $\times 4$ for pustules, $\times 3$ for papules). The inflammatory score was obtained by multiplying the total severity score for each lesion by the inflammatory index and adding the total for all lesions.

2) *Examiner's subjective opinion.* Clinical photographs taken before and after the 2-month treatment provided support for each examiner's subjective opinion (score: unchanged = 1, slight improvement = 2, marked improvement = 3).

3) *Patient's opinion.* Patients were asked to give their own opinion of the result, using the same classification system as the examiner.

Laboratory examinations

Blood samples for plasma and erythrocyte zinc determination were taken in the morning before the treatment period and after the 2-month treatment. Zinc was assayed by flame absorption spectrometry. Hemoglobin, white blood cells, SGOT, SGPT, alkaline phosphatases, triglycerides and cholesterol were analysed at 0, 4, and 8 weeks.

Statistical methods

Statistical evaluations of the results were performed using the Student's and χ^2 -tests.

RESULTS

The mean age of the placebo group was 22 ± 8 years, and that of the zinc group, 22 ± 6 years. There were 22 men and 12 women in the placebo group and 17 men and 15 women in the zinc group. Acne lesions had existed in both groups for 5-6 years. The inflammatory score before the treatment period was 58 ± 32.8 for the placebo group and 49 ± 22.9 for the zinc group ($p < 0.1$ NS).

Table I. Inflammatory score in zinc and placebo groups

Group	n	+Month	Month 1	Month 2
Placebo	34	58 ± 32.8	46 ± 28.7	47 ± 29.8
Zinc	32	49 ± 22.9	34 ± 14.8	27 ± 14.9
				$p < 0.02$

Evaluation of the three scores

1) *Inflammatory score* (Table I). After one month of treatment, scores were 46 ± 29 for the placebo group and 34 ± 15 for the zinc group. After 2 months these scores were 47 ± 30 and 27 ± 15 , respectively ($p < 0.02$).

2) *Examiner's opinion* (Table II). Opinions for the zinc group after 2 months of treatment: no change=8 patients, slight improvement=12, and marked improvement=12. The results for the placebo group were 26, 5 and 3, respectively. Using the scores, the results for the placebo group were $m = 1.3$, $sm = 0.64$, and for the zinc group, $m = 2.1$, $sm = 0.78$ ($t = 4.146$, $p < 10^{-4}$).

3) *Patient's opinion* (Table II). Opinions for the zinc group after 2 months of treatment: no change=12 patients; slight improvement=11 and marked improvement=9. Results for the placebo group: 22, 8 and 4, respectively. So, using the scores, the results for the placebo group were $m = 1.5$, $sm = 0.71$, and for the zinc group, $m = 1.9$, $sm = 0.81$ ($t = 2.36$, $p < 0.002$).

The three scores (inflammatory, examiner's opinion and patient's opinion) thus showed statistically significant differences between the two groups after 2 months of treatment.

Laboratory examinations

Mean plasma zinc concentration increased significantly in the zinc group after 2 months of treatment (before treatment (M0)=951.9 µg/l, after 2 months of treatment (M2)=1 102.6 µg/l; $p = 0.001$). Mean erythrocyte zinc concentration did not increase significantly after the 2-month period (M0=3 433 µg/l, M2=3 474 µg/l, NS). All results of the routine laboratory examinations were normal.

Side effects

Three patients in the placebo group reported nausea. In the zinc group there were also 3 reports of nausea as well as 6 of slight gastralgia and 2 of abdominal pain.

DISCUSSION

The study shows that oral zinc gluconate at a low dose of 0.2 g daily gave significantly better results than a placebo in the treatment of inflammatory acne. In the literature, the results of oral use of zinc have been controversial. This may be due in part to differences in the type of acne treated, whether retentional or inflammatory. Cunliffe et al. (2) in a double-blind trial of zinc and tetracycline, noted that zinc therapy has a significant effect on pustular lesions. It would thus appear that zinc therapy is essentially effective on inflammatory lesions.

The effectiveness of zinc on inflammatory lesions may be attributed to its action on inflammatory cells. The regulatory role of zinc in controlling bactericidal activity, phagocytosis and chemotaxis of granulocytes has been demonstrated (3, 4, 5). Another important factor is the dose of zinc salt used. In the literature the authors gave 400 to 600 mg of zinc sulfate in effervescent zinc sulfate/citrate or zinc sul-

Table II. Evaluation of examiner and patient in the two groups

	Examiner			Patient		
	Improvement			Improvement		
	None	Slight	Marked	None	Slight	Marked
Zinc (n=32)	8	12	12	12	11	9
Placebo (n=34)	26	5	3	22	8	4

fate tablet form. In our study, patients were treated with gluconate (which is often better tolerated by the digestive mucosa than sulfate), at low doses of 200 mg/day. The zinc capsules were given before breakfast to avoid a decrease in zinc absorption due to the food.

In vitro studies, Chvapil et al. (4) and Lennard (5) have demonstrated a parabolic correlation between leukocyte zinc content and phagocyte capacity. The maximum phagocyte capacity of neutrophils appears to correspond to a critical range of serum zinc (4), and low as well as high serum zinc levels can significantly inhibit granulocyte functions in rats (5). These results suggest that different zinc doses may induce different results in acne lesions, and our findings indicate that low doses of zinc gluconate are significantly effective in inflammatory acne. We found an increase in plasma zinc in our zinc group after 2 months of therapy, but with no increase in erythrocyte zinc. This increase in plasma zinc concentration may have had an effect on granulocyte functions and thus on inflammatory lesions.

It may be concluded that this double-blind trial demonstrates the efficiency of low dose of zinc gluconate on specific inflammatory acne lesions.

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